

We claim:

Sub 2¹ 1. A method of producing a red blood cell comprising an agent comprising:

- (a) providing said red blood cell;
- (b) pre-sensitising said red blood cell; and,
- (c) loading said red blood cell with said agent.

5

Sub 2² 2. A method according to claim 1 said step (c) comprising leading a first and said red blood cell with a second agent.

3. A method according to claim 1, further comprising the step of electrosensitising the cell.

10

Sub 2² 4. A method for selectively releasing an agent from a red blood cell comprising the steps of:

- (a) pre-sensitising a red blood cell;
- (b) loading said red blood cell with an agent;
- (c) electrosensitising said red blood cell; and
- (d) effectuating substantial release of said agent from said sensitised red blood cell by applying ultrasound at a frequency and energy sufficient to cause disruption of unsensitised red blood cells,

15

20 5. A method for delivering an agent in a vertebrate comprising,

- (a) pre-sensitising a red blood cell;
- (b) loading said red blood cell with an agent;

(c) electrosensitising said red blood cell;

(d) introducing said red blood cell into a vertebrate; and

(d) releasing said agent from said sensitised cell by ultrasound.

5 6. A method according to claim 5, wherein said red blood cell of step (w) is immunocompatible with said vertebrate.

7. A method according to claim 5, in which the red blood cell is PEGylated prior to being introduced into the vertebrate.

10

8. A method according to claim 5 in which the vertebrate is a mammal.

9. A method according to claim 1 or claim 5 wherein one or both of said pre-sensitising or electrosensitising steps is performed *in vitro* or *ex-vivo*.

15

Sub B8 10. A method according to claim 1 or claim 5, wherein said pre-sensitising step comprises applying an electric field to said red blood cell.

20

Sub a1 11. A method according to claims 1 or claim 5, wherein said pre-sensitising step further comprises applying ultrasound to the red blood cell.

12. A method according to claim 1 or claim 5, wherein said loading step comprises hypotonic dialysis.

13. A method according to claim 3, wherein said electrosensitizing step comprises applying an electric field to said red blood cell.

14. A method according to claim 13, wherein said electric field applied to said red blood cell ranges from 0.1 kV/cm to 10 kV/cm.

15. A method according to claim 13, wherein said electric field is applied to said red blood cell 1 microsecond to 100 milliseconds.

16. A method according to claim 3, wherein said electrosensitisation step is performed after said loading step.

17. A method according to claim 3, wherein said electrosensitisation step is performed before said loading step.

18. A method according to claim 4, wherein said ultrasound is selected from the group consisting of diagnostic ultrasound, therapeutic ultrasound and a combination of diagnostic and therapeutic ultrasound.

19. A method according to claim 4 wherein the applied ultrasound energy source is at a power level from about 0.05 W/cm² to about 100 W/cm².

20. A red blood cell composition comprising a plurality of pre-sensitized red blood cells.

21. The red blood cell composition according to claim 20, wherein said red blood cell is pre-sensitized to permit loading of an agent.

22. A red blood cell composition according to claim 20 comprising a plurality of pre-sensitized electro sensitized red blood cells.

23. A red blood cell composition according to claim 20, wherein said red blood cells are immunocompatible in a vertebrate.

24. A red blood cell composition according to claim 20 wherein said agent is selected from a group consisting of: a protein, a polypeptide, a peptide, a nucleic acid, a peptide nucleic acid (PNA), a virus, a nucleotide, a ribonucleotide, a deoxyribonucleotide, a heteroduplex, a nanoparticle, an amino acid, a steroid, a proteoglycan, a lipid, a fatty acid, an oligosaccharide, a glycoprotein, and a carbohydrate.

25. A red blood cell composition according to claim 24 wherein said agent further comprises an imaging agent.

26. A red blood cell composition obtainable by a method comprising:

- (a) presensitising a red blood cell;
- (b) loading the cell with an agent; and
- (c) electrosensitising the cell.

27. A kit comprising a red blood cell composition according to claim 20, and packaging materials therefor.

28. A kit comprising a pre-sensitised red blood cell, an agent, and packaging materials therefor.

29. A kit according to claim 27 or 28, said kit further comprising a liquid selected from the group consisting of: a buffer, diluent, an excipient, a saline buffer, a physiological buffer, serum, and plasma.

30. A pharmaceutical composition comprising a red blood cell composition made by a process comprising:

- (a) providing a red blood cell;
- (b) pre-sensitizing said red blood cell;
- (c) loading said red blood cell with an agent; and
- (d) electrosensitizing said red blood cell.

31. The composition of claim 31 wherein said red blood cell composition further comprises a red blood cell is immunocompatible in a vertebrate.

32. The composition of claim 31 wherein said red blood cell comprises PEG.

33. A device for producing a red blood cell delivery composition, comprising:

- (a) one or more flow cells and electrosensitisation means;
- (b) one or more dialysis systems;

in which the flow cell is linked to the dialysis system by connecting means capable of allowing transfer of red blood cells from the flow cell to the dialysis system.

A device as
ultrasound

ultr

Gold Bid